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Antibiotic Resistance Pattern In Two Nigerian Tertiary Hospitals

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ABSTRACT

Antibiotics are among the most widely used drugs to treat patients with various diseases in public and private health institutions. It`s use has been found to be associated with various degrees of antibiotic resistance leading to difficulty in managing these various morbidities. The resistance pattern has been found to co-relate strongly with the pattern of antibiotic use. The study is a retrospective study which aimed at studying the resistance pattern to various antibiotics in two Nigerian teaching hospitals located at different geographical areas of the country. The study aimed at determining the factors associated with increased resistance to antibiotics. The pattern of resistance was found to be higher in the rejoin with more frequent use of antibiotics and some recommendations were proposed as a measure of reducing antibiotic resistance to the barest minimum.

Key Words: Antibiotic, Resistance pattern, Nigerian, Tertiary Hospitals.

INTRODUCTION

Use of antibacterial drugs over the last 60years has triggered a combination of genetic and biochemical mechanisms within the bacteria to secure their survival in environments where antibiotics are present (Dzidic et al. 2008). Bacterial clones with natural and acquired resistance (Michael et al 1999) have continuously been selected as an evolutionary trend to the use of antibiotics (Uppsala et al 2004).

Resistance can be acquired as a result of genetic events causing alteration in the pre-existing bacterial genome, such as point mutation and gene amplifications. The other major mechanism is horizontal gene transfer between species where transposons, integrons or plasmids are introduced into an organism (Mordi et al. 2008). Resistance development is a natural biological outcome of antibiotic use (Otto Cars et al. 2005). The more we use these drugs the more we increase the speed of emergence and selection of resistant bacteria. In different parts of the world, especially in the underdeveloped rejoins of the world, there is an extensive overuse of antibiotics e.g. use based on incorrect medical indication as well as misuse by prescribing the wrong agent, administration route, dose and treatment duration (Cail Lior et al. 2014).

When antibiotics are used too often in sub-optimal dosages, bacteria have been reported to become resistant to them. This is a serious concern to public health policy makers; the result is treatment failure when patients suffering from serious infections take these antibiotics. The pattern of resistance has been found to correlate strongly with the pattern of drug use (Okeke et al. 2000). The effect of this is that apart from diagnostic dilemma, the factors influencing how antibiotics are used are many and complex (Nordberg et al. 2003). This is because commonly used antibiotics are almost going out of use due to rapid development of resistance against them. This is against the backdrop in the reduced rate of development of new antimicrobial agents against this emerging trend of antibiotic resistance.

The study looked at antibiotic resistance patterns in two hospitals in Nigeria. The two hospitals are situated in two different geographical regions of Nigeria and the indigenes are made up of people of different socio-cultural backgrounds.

MATERIAL AND METHODS

Study Setting:

This was a retrospective study carried out in two (2) teaching hospitals in Nigeria. The first institution was the University of Benin Teaching Hospital (UBTH) which is located in Benin city, the capital of Edo state, in the South-south region. It is a 628 bed tertiary institution in Edo State serving as a referral centre for hospitals both in Edo state and parts of the surrounding Delta and Ondo States.

The second institution was Usman Danfodio University Teaching Hospital (UDUTH) which is located in Sokoto, the capital of Sokoto State in the North-western part of Nigeria. It is a 548 bed tertiary institution serving as a referral centre for hospitals in Sokoto and the surrounding Kebbi and Zamfara States.

Study design.

An evaluation of antibiotic sensitivity in each hospital using records in the microbiology laboratories over a five year period (2003-2007) was done.

Antibiotic Resistance Pattern.

Records of sensitivity and resistance to antibiotics in the Microbiology laboratory of both hospitals over a five-year period (2003-2007) were obtained from the laboratory result database of their respective departments of Microbiology. The report of microbiology results of Wound swab, Cerebrospinal fluid, Stool, Blood, Urine and Sputum were obtained and analyzed. The number resistant to a particular antibiotic was recorded against the number sensitive to it and the percentage resistance calculated using the formula (R/R+S×100/1).

Data Analysis

All data obtained were recorded in a proforma. The data were entered into a computer and analyzed using statistical package for social sciences (SPSS) software version 15.0 for windows. Statistical tests of significance were done using chi-square test, statistical significance was set at $P \leq 0.05$.

Cross tabulations and bivariate analysis was done with P-values, odds ratio and with 95% confidence intervals determined where necessary. Results were tabulated.

Ethical Approval

Ethical approval for the study was sought and obtained from the Ethical Committee of both Hospitals.

RESULT AND DISCUSSION

Antibiotic resistance has been a worldwide problem that is likely going to affect health care delivery very seriously and resistance development has been found to be strongly related to the pattern of use, for example, use without any justifiable reason, under dosing of antibiotics as well as use of fake antibiotics.

The resistance patterns of both hospitals displayed showed variation on the organisms isolated in both laboratories, this may be a reflection of the level of standardization of the different laboratories, however the resistance profile of the same organism isolated still showed that resistance is higher to the same antibiotic in UBTH than in UDUTH .For example tables 1 and 6 showed the values of percentage resistance in both hospitals in 2003. Commonly used antibiotics in the past like co- trimoxazole, tetracycline cloxacillin and ampicillin showed higher values of percentage resistance than the more recent antibiotics like ciprofloxacin, ofloxacin, ceftriazone and collistin sulphate. This trend was replicated in the subsequent years up to 2007.

Table 1:
Number of Different Bacterial Species Isolated from Various Specimens and tested Against the indicated Antibiotics at the University of Benin Teaching Hospital, Nigeria in 2003 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	AUG	CXM	CRO	CAZ	OFX	CN	AMX	E	OB	SXT	TE	C
Staphylococcus *aureus*	190	20%	22%	25%	20%	26%	36%	38%	50%	60%	81.5 %	91%	91%	70%
Klebsiella *pneumonia*	55	18%	24%	50%	18%	18%	38%	60%	90%	92%	98%	100%	80%	80%
Proteus *Mirabilis*	50	36%	30%	36%	28%	20%	35%	40%	88%	90%	92%	90%	100%	65%
Pseudomonas *aeruginosa*	30	20%	97%	93%	30%	20%	32%	68%	98%	100%	96%	100%	90%	96.5%
Streptoccocus *pneumonia*	20	30%	20%	30%	20%	10%	30%	48%	60%	85%	98%	85%	100%	100%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates.
AUG = Amoxicillin Clavulanate CN = Gentamycin SXT = Co trimoxazole CXM = Cefuroxime AMX = Amoxicillin TE = Tetracycline CAZ = Ceftazidime CRO = Ceftriazone, ER = Erythromycin CR = Chloramphenicol OFX = Ofloxacin, CIP=Ciprofloxacin and OB Cloxacillin values represent the percentage of isolates Resistant to the indicated antibiotic

Table 2:
Number of Different Bacterial Species Isolated from various Specimens and tested against the indicated Antibiotics at the University of Benin Teaching Hospital, Nigeria in 2004 and their Percentage Resistance

Bacteria	No. of Isolates	CIP	AUG.	CXM	CRO	CAZ	OFX	CN	AMX	E	OB	SXT	TE	C
Staphylococcus *aureus*	200	22 %	22%	28%	20%	40 %	36 %	38 %	48%	60%	80%	90%	92%	70%
Klebsiella *pneumonia*	55	18 %	28%	45%	18%	20 %	32 %	65 %	91%	94%	98%	100 %	100 %	96%
Pseudomonas *aeruginosa*	38	34 %	100 %	100 %	50%	16 %	34 %	66 %	100 %	100 %	100 %	100 %	100 %	100 %
Streptoccus *pneumonia*	36	19 %	30%	30%	29%	14 %	35 %	50 %	80%	85%	98%	80%	96%	75%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates.
Aug = Amoxicillin Clavulanate CN = Gentamycin SXT = Cotrimoxazole CXM = Cefuroxime, AMX = Amoxicillin, TE = Tetracycline, CAZ = Ceftazidime, CRO = Ceftriazone, E = Erythromycin, CR = Chloramphenicol, OFX = Ofloxacin, CIP= Ciprofloxacin and OB Cloxacillin. values represent the percentage of isolates Resistant to the indicated antibiotic.

Table 3:
Number of Different Bacterial Species isolated from various Specimens and tested against the indicated Antibiotics at the University of Benin Teaching Hospital, Nigeria in 2005 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	AUG	CXM	CRO	CAZ	OFX	CN	AMX	E	OB	SXT	TE	C
Staphylococcus *aureus*	185	22%	24%	26%	22%	40%	38%	30%	50%	58%	80%	88%	90%	70%
Klebsiella *pneumonia*	68	28%	30%	45%	28%	30%	35%	65%	90%	92%	100 %	78%	100%	96%
Pseudomonas *aeruginosa*	50	40%	100 %	100%	40%	40%	38%	60%	100%	100 %	100 %	100 %	100%	100 %
Streptoccocus *pneumonia*	40	28%	32%	28%	26%	30%	28%	45%	80%	85%	98%	80%	96%	75%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates.
Aug = Amoxicillin Clavulanate, CN = Gentamycin, SXT = Cotrimoxazole, CXM = Cefuroxime, AMX = Amoxicillin, TE = Tetracycline, CAZ = Ceftazidime, CRO = Ceftriazone, ER = Erythromycin, CR = Chloramphenicol, OFX = Ofloxacin, CIP = Ciprofloxacin and OB Cloxacillin. values represent the percentage of isolates **Resistant** to the indicated antibiotic.

Table 4:
Number of different Bacterial Species isolated from various Specimens and tested against the indicated Antibiotics isolated at the University of Benin Teaching Hospital, Nigeria in 2006 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	AUG.	CX M	CRO	CAZ	OFX	CN	AM X	E	OB	SXT	TE	C
Staphylococcus *aureus*	210	18%	20%	30%	30%	35%	40%	38%	48%	58%	80%	90%	91%	70%
Klebsiella *pneumonia*	80	25%	30%	50%	18%	20%	38%	70%	90%	93%	100%	98%	100%	96%
Proteus *Mirabilis*	75	32%	32%	35%	24%	22%	40%	38%	88%	90%	98%	88%	94%	72%
Pseudomonas *aeruginosa*	60	30%	30%	100 %	25%	20%	30%	70%	100 %	100 %	100%	100%	100%	100 %
Streptoccocus *pneumonia*	55	69%	100%	30%	14%	15%	30%	50%	85%	80%	100%	80%	95%	75%

Values of the percentages were got from the number of isolates resistant to the indicated antibiotic over the total number of isolates.

Aug = Amoxicillin Clavulanate, CN = Gentamycin, SXT = Cotrimoxazole, CXM = Cefuroxime, AMX = Amoxicillin, TE = Tetracycline, CAZ = Ceftazidime, CRO = Ceftriazone, ER = Erythromycin, CR = Chloramphenicol, OFX = Ofloxacin, CIP = Ciprofloxacin and OB Cloxacillin. values represent the percentage of isolates **Resistant** to the indicated antibiotic.

Table 5:
Number of Different Bacterial Species Isolates from various Specimens and tested against the indicated Antibiotics at the University of Benin Teaching Hospital, Nigeria in 2007 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	AUG	CXM	CRO	CAZ	OFX	CN	AMX	E	OB	SXT	TE	C
Staphylococcus *aureus*	175	20%	22%	30%	28%	35%	38%	40%	50%	35%	80%	88%	90%	70%
Klebsiella *pneumonia*	70	17%	26%	40%	18%	20%	35%	65%	92%	93%	100 %	100 %	100%	96%
Proteus *Mirabilis*	65	20%	35%	40%	20%	15%	40%	35%	85%	88%	98%	88%	94%	72%
Escherichia *coli*	70	22%	22%	40%	24%	20%	30%	70%	88%	90%	98%	97%	100%	100 %
Pseudomonas *aeruginosa*	60	35%	100 %	100%	22%	20%	35%	70%	100%	100 %	100 %	100 %	100%	75%
Streptoccocus *pneumonia*	50	28%	30%	28%	12%	15%	28%	50%	80%	85%	100 %	85%	95%	74%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates.

Aug = Amoxicillin Clavulanate, CN = Gentamycin, SXT = Cotrimoxazole, CXM = Cefuroxime, AMX = Amoxicillin, TE = Tetracycline), CAZ = Ceftazidime, CRO = Ceftriazone, E = Erythromycin CR = Chloramphenicol, OFX = Ofloxacin, CIP=Ciprofloxacin and OB Cloxacillin. values represent the percentage of isolates **Resistant** to the indicated antibiotic

Table 6:
Number of different Bacterial Species isolated from various Specimens and tested against the indicated Antibiotics at the Usman Danfodiyo University Teaching Hospital Sokoto, Nigeria in 2003 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	OFX	CRO	AUG	CN	TE	AMX	NA	SXT	N	E	AMP	OB	COL
Staphylococcus *aureus*	118	8%	7%	20%	9%	28%	79%	47%	100%	75%	33%	57%	86%	82%	3%
Escherichia *coli*	98	17 %	20%	20%	11%	27%	91%	58%	29%	90%	24%	90%	89%	100%	2%
Streptococcus *pneumonia*	88	8%	8%	2%	35%	70%	97%	52%	100%	97%	75%	77%	67%	91%	98%
Pseudomonas *aeruginosa*	30	10 %	27%	14%	83%	27%	95%	67%	100%	95%	67%	50%	95%	100%	50%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates.
Aug = Amoxicillin Clavulanate, CN = Gentamycin, SXT = Cotrimoxazole, AMX = Amoxicillin, TE = Tetracycline, CRO = Ceftriazone, E = Erythromycin, OFX = Ofloxacin, CIP = Ciprofloxacin, NA = Nalidix Acid, N = Nitrofurantoin, AMP = Ampicillin, COL = Collistin Sulphate and OB Cloxacillin . values represent the percentage of isolates resistant to the indicated antibiotic.

Table 7:
Number of Different Bacterial Species isolated from various Specimens and tested against the indicated Antibiotics at the Usman Danfodiyo University Teaching Hospital Sokoto, Nigeria in 2004 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	OFX	CRO	AUG	CN	TE	AMX	NA	SXT	N	E	AMP	OB	COL
Staphylococcus *aureus*	122	12%	16%	22%	10%	30%	80%	47%	100%	80%	32%	56%	90%	84%	6%
Escherichia *coli*	92	18%	20%	24%	11%	27%	95%	58%	29%	92%	25%	80%	90%	100%	2%
Streptococcus *pneumonia*	104	8%	10%	6%	36%	70%	98%	52%	98%	96%	75%	78%	64%	90%	92%
Pseudomonas *aeruginosa*	36	11%	25%	19%	84%	28%	97%	67%	100%	94%	69%	53%	100%	100%	56%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates

Aug = Amoxicillin Clavulanate, CN = Gentamycin, SXT = Cotrimoxazole, AMX = Amoxicillin, TE = Tetracycline, CRO = Ceftriazone, ER = Erythromycin, OFX = Ofloxacin, CIP = Ciprofloxacin, NA = Nalidix Acid, NI = Nitrofurantoin, AMP = Ampicillin, COL = Collistin Sulphate and OB Cloxacillin . values represent the percentage of isolates resistant to the indicated antibiotic

Table 8:
Number of Different Bacterial Species isolated from various Specimens and tested against the indicated Antibiotics at the Usman Danfodiyo University Teaching Hospital Sokoto, Nigeria in 2005 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	OFX	CRO	AUG	CN	TE	AMX	NA	SXT	N	E	AMP	OB	COL
Staphylococcus *aureus*	132	12%	12%	22%	14%	30%	86%	50%	96%	78%	36%	60%	90%	88%	6%
Escherichia *coli*	104	20%	22%	20%	11%	27%	90%	58%	32%	92%	25%	80%	90%	100%	4%
Streptococcus *pneumonia*	101	10%	12%	6%	36%	70%	96%	56%	100%	96%	78%	76%	64%	91%	96%
Pseudomonas *aeruginosa*	38	12%	26%	13%	84%	29%	97%	68%	100%	89%	68%	53%	100%	100%	50%

Table 9:
Number of Different Bacterial Species isolated from various Specimens and tested against the indicated Antibiotics at the Usman Danfodiyo University Teaching Hospital Sokoto, Nigeria in 2006 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	OFX	CRO	AUG	CN	TE	AMX	NA	SXT	N	E	AMP	OB	COL
Staphylococcus *aureus*	130	8%	8%	20%	9%	28%	79%	47%	100%	75%	34%	58%	86%	84%	4%
Escherichia *coli*	97	17%	20%	20%	11%	27%	92%	58%	29%	92%	25%	80%	90%	100%	2%
Streptococcus *pneumonia*	102	8%	9%	4%	36%	70%	98%	56%	100%	96%	75%	77%	67%	91%	98%
Pseudomonas *aeruginosa*	34	9%	26%	14%	82%	26%	94%	67%	100%	94%	69%	50%	94%	100%	53%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates

Aug = Amoxicillin Clavulanate, CN = Gentamycin, SXT = Cotrimoxazole, AMX = Amoxicillin, TE = Tetracycline, CRO = Ceftriazone, ER = Erythromycin, OFX = Ofloxacin, CIP = Ciprofloxacin, NA = Nalidix Acid, NI = Nitrofurantoin, AMP = Ampicillin, COL = Collistin Sulphate and OB Cloxacillin . values represent the percentage of isolates resistant to the indicated antibiotic

Table 10:
Number of Different Bacterial Species isolated from various Specimens and tested against the indicated Antibiotics at the Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria in 2007 and their Percentage Resistance.

Bacteria	No. of Isolates	CIP	OFX	CRO	AUG	CN	TE	AMX	NA	SXT	N	E	AMP	OB	COL
Staphylococcus *aureus*	120	14%	16%	24%	16%	32%	90%	50%	90%	100%	40%	60%	88%	90%	8%
Escherichia *coli*	99	20%	20%	20%	12%	28%	90%	52%	34%	94%	30%	84%	90%	100%	4%
Streptococcus *pneumonia*	98	14%	12%	8%	36%	70%	90%	56%	98%	96%	78%	76%	64%	91%	91%
Pseudomonas *aeruginosa*	30	10%	27%	13%	83%	30%	97%	67%	100%	90%	67%	53%	100%	100%	50%

Values of the percentages were obtained from the number of isolates resistant to the indicated antibiotic over the total number of isolates.

Aug = Amoxicillin Clavulanate, CN = Gentamycin, SXT = Cotrimoxazole, AMX = Amoxicillin, TE = Tetracycline, CRO = Ceftriazone, ER = Erythromycin, OFX = Ofloxacin, CIP = Ciprofloxacin, NA = Nalidix Acid, NI = Nitrofurantoin, AMP = Ampicillin, COL = Collistin Sulphate and OB Cloxacillin. Values represent the percentage of isolates resistant to the indicated antibiotic.

This may be due to the use profile which was noted to be higher in the study in UBTH than in UDUTH. This supports the finding by Ehimmidu et al (2003) in Zaria where the prevalence of antibiotic resistance was found to be higher among the group that had the highest exposure.

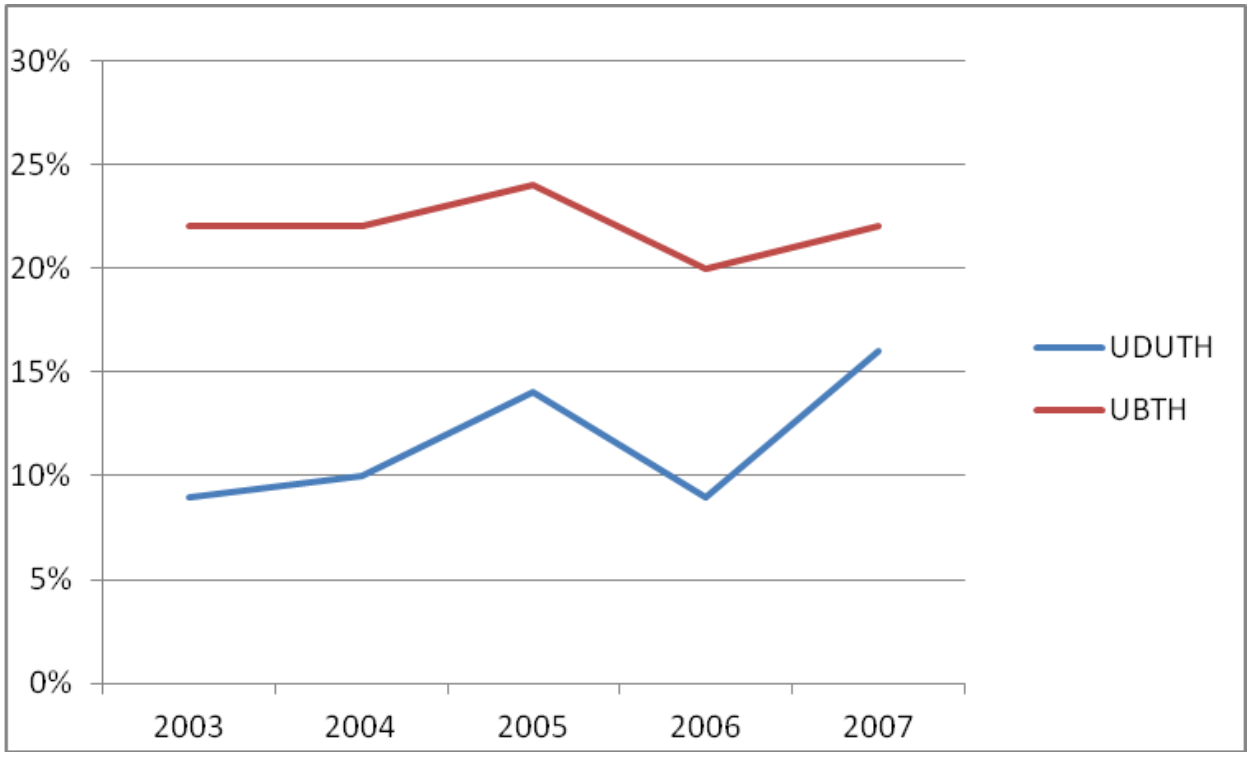

Figure 1: Percentage resistance of *Streptococcus pneumonia* to Augmentin over a 5-year period in both Institutions.

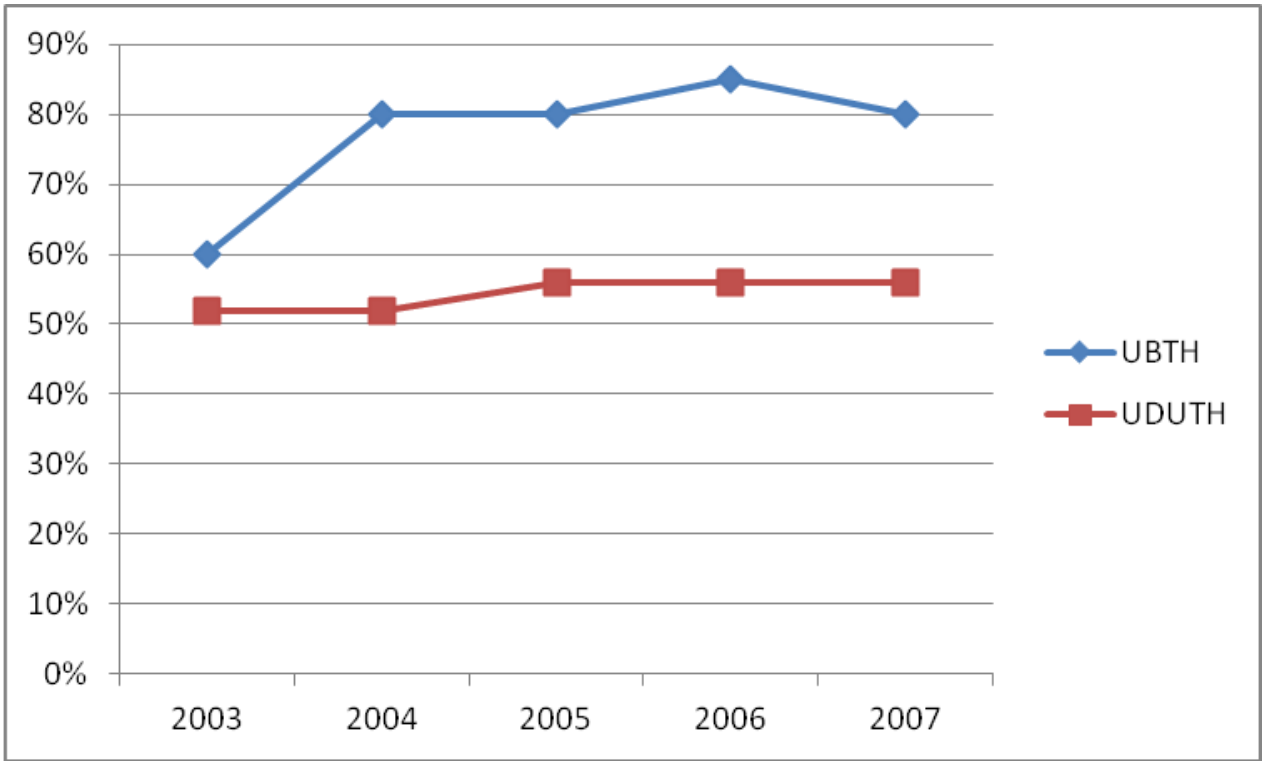

Figure 2: Percentage resistance of *Streptococcus pneumonia* to amoxicillin over a 5-year period in both Institutions

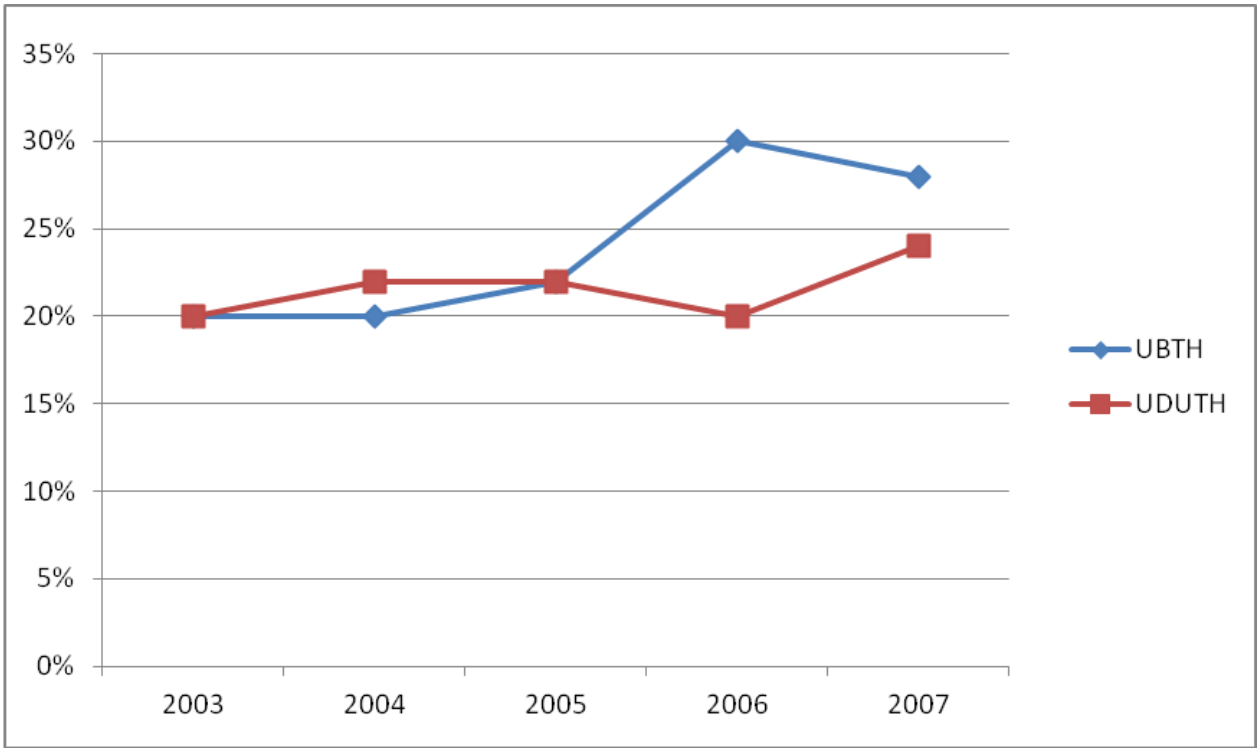

Figure 3: Gradual increase of resistance by *Staphylococcus aureus* to ceftriazone over a 5-year period in both Institutions

For example, figure 1 showed the same trend in resistance development, but UBTH showed higher percentage resistance of *Streptococcus pneumonia* to Augmentin over a 5-year period when compared to UDUTH. In figure 2 the percentage resistance of the same organism to Amoxicillin was much higher but almost similar in trend to that of figure 1. The figure however showed a gradual increase in resistance to Ceftriazone by Staphylococcus *aureus* over the five year period in both hospitals.

The finding of high resistance to the commonly used antibiotics in the past (i.e) cloxacillin, tetracycline and cotrimoxazole in both hospitals was similar to the study by Yismaw et al (2006), Randrianirina et al (2007) and Hawkey (2008) which showed high development of resistance to these same antibiotics that were used in the treatment of Shigellosis at Gondar University hospital North West Ethiopia. However, the study by Okpara et al (2016) in Benin City showed that prolonged hospital stay with associated prolonged use of antibiotics may be responsible for increased drug resistance in the Southern part of Nigeria in comparison to the Northern part. The same study noted that open prescriptions which were more common in the same Southern zone also led to increased dug resistance (Okpara et al. 2016).

Study done by Obaseki-Ebor et al (1987) in Benin City showed that Ampicillin was the most commonly prescribed antibiotics in the past decades and this may explain why Ampicillin is no longer the most commonly prescribed antibiotics in recent times, possibly because of the development of increased resistance to it due to excessive use in the past. A previous study by Nohammad Reza Pourshaf (2007) in Iran showed that the rate of antibiotic resistance among *Pseudomonas aeruginosa* increased significantly in the last decade, with no changes in the ribotype and serotype patterns.

Michael et al in a book titled the Springer, noted that efforts, however has lagged behind good intentions as inappropriate use of antimicrobials remains the norm rather than the exception in most developing world as well as in many industrialized countries (Michael et al. 2010).

It was also noted from the study that the antibiotic Nalidixic acid commonly used for urinary tract infection, had high percentage of resistance in the North- West while its use was

almost completely absent in the South- South region. This may be explained by the fact that UTI may be more common in the North-West than in the South-South and the fact that they do not circumcise their male children till adulthood may be a contributory factor. The increased/prolonged use of antibiotics noted above can also be related to the increased resistance seen in the study done at UBTH.

RECOMMENDATIONS.

There is an urgent need for greater regulation of antimicrobial distribution and sale so that private shops staffed by untrained owners and employees are no longer a common source of antimicrobials.

Enhanced educational outreach to both consumers and health-care providers to change the pattern of antimicrobial use is crucial in addition to implementing and sustaining resistance surveillance systems that will alert the medical and public health communities to changes in resistance is also crucial. More checks and balances to fight against production and sale of fake and substandard drugs should be put in place, in addition to policies to ensure sale of antibiotics only on prescription to avoid indiscriminate use.

CONCLUSION.

The percentage pattern of antibiotic resistance was found to be higher at UBTH than at UDUTH which correlates with the initial study that found that UBTH had more frequent as well as prolonged use of antibiotics than UDUTH.

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